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=> e fearnley i m, 2001/re

E1	9	FEARNLEY I M, 1994, V22, P551, BIOCHEM SOC T/RE
E2	16	FEARNLEY I M, 1996, V24, P912, BIOCHEM SOC T/RE
E3	0 -->	FEARNLEY I M, 2001/RE
E4	1	FEARNLEY I M, 2001, IN PRESS J BIOL CHEM/RE
E5	1	FEARNLEY I M, 2001, V24, P24, J HIRST J BIOL CHEM/RE
E6	90	FEARNLEY I M, 2001, V276, P38345, J BIOL CHEM/RE
E7	2	FEARNLEY I M, 2006, V357, P103, METHOD MOL BIOL/RE
E8	1	FEARNLEY I M, 2007, V357, P103, METHOD MOL BIOL/RE
E9	20	FEARNLEY I R, 1987, V105, P1550, ARCH OPHTHALMOL-CHIC/RE
E10	2	FEARNLEY I R, 1987, V105, P649, ARCH OPHTHALMOL-CHIC/RE
E11	5	FEARNLEY I R, 1988, V72, P636, BR J OPHTHALMOL/RE
E12	1	FEARNLEY I R, 1988, V72, P636, BR J OPHTHALMOL/RE

=> s e4 e6

L1 0 "FEARNLEY I M, 2001, IN PRESS J BIOL CHEM"/RE "FEARNLEY I M,
2001, V276, P38345, J BIOL CHEM"/RE

=> s e4 or e6

L2 187 "FEARNLEY I M, 2001, IN PRESS J BIOL CHEM"/RE OR "FEARNLEY I M,
2001, V276, P38345, J BIOL CHEM"/RE

=> s l2 and electr?

L3 93 L2 AND ELECTR?

=> s l2 and electrode?

L4 4 L2 AND ELECTRODE?

=> s l3 and pd<20030328

L5 34 L3 AND PD<20030328

=> s l5 and (nad# or nicotinamide or pyridine)

L6 27 L5 AND (NAD# OR NICOTINAMIDE OR PYRIDINE)

=> dup rem l6

PROCESSING COMPLETED FOR L6

L7 20 DUP REM L6 (7 DUPLICATES REMOVED)
ANSWERS '1-9' FROM FILE SCISEARCH
ANSWERS '10-20' FROM FILE CAPLUS

=> d bib abs 1-20

L7 ANSWER 1 OF 20 SCISEARCH COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 1

AN 2003:157871 SCISEARCH Full-text

GA The Genuine Article (R) Number: 644JW

TI Involvement of tyrosines 114 and 139 of subunit NuoB in the proton pathway
around cluster N2 in Escherichia coli NADH : ubiquinone
oxidoreductase

AU Flemming D; Hellwig P; Friedrich T (Reprint)

CS Univ Freiburg, Inst Organ Chem & Biochem, Albertstr 21, D-79104 Freiburg,
Germany (Reprint); Univ Freiburg, Inst Organ Chem & Biochem, D-79104
Freiburg, Germany; Univ Frankfurt, Inst Biophys, D-60590 Frankfurt,
Germany

CYA Germany

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (31 JAN 2003) Vol. 278, No. 5,
pp. 3055-3062.
ISSN: 0021-9258.

PB AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE,
BETHESDA, MD 20814-3996 USA.

DT Article; Journal

LA English

REC Reference Count: 44

ED Entered STN: 28 Feb 2003

Last Updated on STN: 28 Feb 2003

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The proton-pumping NADH:ubiquinone oxidoreductase (complex I) couples
the transfer of electrons from NADH to ubiquinone with the translocation
of protons across the membrane. Electron transfer is accomplished by FMN
and a series of iron-sulfur clusters. Its coupling with proton
translocation is not yet understood. Here, we report that the redox
reaction of the FeS cluster N2 located on subunit NuoB of the
Escherichia coli complex I induces a protonation/deprotonation of
tyrosine side chains. Electrochemically induced FT-IR difference spectra
revealed characteristic tyrosine signals at 1,515 and 1,498 cm⁻¹ for the
protonated and deprotonated form, respectively. Mutants of three
conserved tyrosines on NuoB were generated by complementing a
chromosomal in-frame deletion strain with nuoB on a plasmid. Though the
single mutations did not alter the electron transport activity of
complex I, the EPR signal of cluster N2 was slightly shifted. The
tyrosine signals detected by FT-IR spectroscopy were roughly halved in
the mutants Y114C and Y139C while only minor changes were detected in
the Y154H mutant. The enzymatic activity of the Y114C/Y139F double
mutant was 80% reduced, and FT-IR difference spectra of the double
mutant revealed a complete loss the modes characteristic for protonation
reactions of tyrosines. Therefore, we propose that tyrosines 114 and
139 on NuoB were protonated upon reduction of cluster N2 and were thus
involved in the proton-transfer reaction coupled with its redox
reaction.

L7 ANSWER 2 OF 20 SCISEARCH COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 2

AN 2003:112302 SCISEARCH Full-text

GA The Genuine Article (R) Number: 638JY

TI The ND5 subunit was labeled by a photoaffinity analogue of fenpyroximate
in bovine mitochondrial complex I

AU Nakamaru-Ogiso E; Sakamoto K; Matsuno-Yagi A; Miyoshi H; Yagi T (Reprint)

CS Scripps Res Inst, Dept Mol & Expt Med, Div Biotechnol, La Jolla, CA 92037
USA (Reprint); Kyoto Univ, Grad Sch Agr, Div Appl Life Sci, Kyoto 6068502,
Japan

CYA USA; Japan

SO BIOCHEMISTRY, (26 JAN 2003) Vol. 42, No. 3, pp. 746-754.

ISSN: 0006-2960.

PB AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.

DT Article; Journal

LA English

REC Reference Count: 75

ED Entered STN: 14 Feb 2003

Last Updated on STN: 14 Feb 2003

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Fenpyroximate is a potent inhibitor of the mitochondrial proton-translocating NADH-quinone oxidoreductase (complex I). We synthesized its photoaffinity analogue [H-3](trifluoromethyl)phenyldiaz irinylfenpyroximate ([H-3]TDF). When bovine heart submitochondrial particles (SMP) were illuminated with UV light in the presence of [H-3]TDF, radioactivity was mostly incorporated into a 50 kDa band. There was a good correlation between radioactivity labeling of the 50 kDa band and inhibition of the NADH oxidase activity, indicating that a 50 kDa protein is responsible for the inactivation of complex I. Blue native gel electrophoresis of the [H-3]TDF-labeled SNIP revealed that the majority of radioactivity was found in complex I. Analysis of the complex I band on an SDS gel showed a major peak of radioactivity at similar to 50 kDa. There are three subunits in complex I that migrate in this region: FP51K, IP49K, and ND5. Further analysis using the 2D gel electrophoresis implied that the labeled protein was the ND5 subunit. Labeling of the ND5 subunit was stimulated by NADH /NADPH but was prevented by various complex I inhibitors. Amiloride derivatives that are known to be inhibitors of Na⁺/H⁺ antiporters also diminished the labeling. In agreement with the protective effect, we observed that the amiloride derivatives inhibited NADH-ubiquinone-1 reductase activity but not NADH-K3Fe(CN)(6) reductase activity in bovine SMP. These results suggest that the ND5 subunit is involved in construction of the inhibitor- and quinone-binding site(s). Furthermore, it seems likely that the ND5 subunit may participate in H⁺(Na⁺) translocation in coupling site 1.

L7 ANSWER 3 OF 20 SCISEARCH COPYRIGHT (c) 2008 The Thomson Corporation on STN DULPLICATE 3

AN 2003:317327 SCISEARCH Full-text

GA The Genuine Article (R) Number: 665NV

TI Analysis of the subunit composition of complex I from bovine heart mitochondria

AU Carroll J; Fearnley I M; Shannon R J; Hirst J; Walker J E (Reprint)

CS MRC, Dunn Human Nutr Unit, Hills Rd, Wellcome Trust MRC Bldg, Cambridge CB2 2XY, England (Reprint); MRC, Dunn Human Nutr Unit, Cambridge CB2 2XY, England

CYA England

SO MOLECULAR & CELLULAR PROTEOMICS, (FEB 2003) Vol. 2, No. 2, pp. 117-126.

ISSN: 1535-9476.

PB AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA.

DT Article; Journal

LA English

REC Reference Count: 55

ED Entered STN: 25 Apr 2003

Last Updated on STN: 25 Apr 2003

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Complex I purified from bovine heart mitochondria is a multisubunit membrane-bound assembly. In the past, seven of its subunits were shown

to be products of the mitochondrial genome, and 35 nuclear encoded subunits were identified. The complex is L-shaped with one arm in the plane of the membrane and the other lying orthogonal to it in the mitochondrial matrix. With mildly chaotropic detergents, the intact complex has been resolved into various subcomplexes. Subcomplex I λ represents the extrinsic arm, subcomplex I α consists of subcomplex I λ plus part of the membrane arm, and subcomplex I β is another substantial part of the membrane arm. The intact complex and these three subcomplexes have been subjected to extensive reanalysis. Their subunits have been separated by three independent methods (one-dimensional SDS-PAGE, two-dimensional isoelectric focusing/SDS-PAGE, and reverse phase high pressure liquid chromatography (HPLC)) and analyzed by tryptic peptide mass fingerprinting and tandem mass spectrometry. The masses of many of the intact subunits have also been measured by electrospray ionization mass spectrometry and have provided valuable information about post-translational modifications. The presence of the known 35 nuclear encoded subunits in complex I has been confirmed, and four additional nuclear encoded subunits have been detected. Subunits B16.6, B14.7, and ESSS were discovered in the SDS-PAGE analysis of subcomplex I λ , in the two-dimensional gel analysis of the intact complex, and in the HPLC analysis of subcomplex I α , respectively. Despite many attempts, no sequence information has been obtained yet on a fourth new subunit (mass 10,566 \pm 2 Da) also detected in the HPLC analysis of subcomplex I β . It is unlikely that any more subunits of the bovine complex remain undiscovered. Therefore, the intact enzyme is a complex of 46 subunits, and, assuming there is one copy of each subunit in the complex, its mass is 980 kDa.

L7 ANSWER 4 OF 20 SCISEARCH COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 4

AN 2002:440168 SCISEARCH Full-text

GA The Genuine Article (R) Number: 553PR

TI A novel, enzymatically active conformation of the Escherichia coli
NADH : ubiquinone oxidoreductase (complex I)

AU Bottcher B; Scheide D; Hesterberg M; Nagel-Steger L; Friedrich T (Reprint)

CS Univ Freiburg, Inst Org Chem & Biochem, Albertstr 21, D-79104 Freiburg,
Germany (Reprint); European Mol Biol Lab, Struct Biol & Biocomp Programme,
D-69117 Heidelberg, Germany; Univ Dusseldorf, Inst Phys Biol, D-40225
Dusseldorf, Germany

CYA Germany

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (17 MAY 2002) Vol. 277, No. 20,
pp. 17970-17977.
ISSN: 0021-9258.

PB AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE,
BETHESDA, MD 20814-3996 USA.

DT Article; Journal

LA English

REC Reference Count: 41

ED Entered STN: 7 Jun 2002

Last Updated on STN: 7 Jun 2002

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Electron microscopy has demonstrated the unusual L-shaped structure of the respiratory complex I consisting of two arms, which are arranged perpendicular to each other. We found that the Escherichia coli complex I has an additional stable conformation, with the two arms arranged side by side, resulting in a horseshoe-shaped structure. The structure of both conformations was determined by means of electron microscopy of gold thioglucose-stained single particles. They were distinguished from each other by titration of the complex with polyethylene glycol and by

means of analytical ultracentrifugation. The transition between the two conformations is induced by the ionic strength of the buffer and is reversible. Only the horseshoe-shaped complex I exhibits enzyme activity in detergent solution, which is abolished by the addition of salt. Therefore, it is proposed that this structure is the native conformation of the complex in the membrane.

L7 ANSWER 5 OF 20 SCISEARCH COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 5

AN 2002:665182 SCISEARCH [Full-text](#)

GA The Genuine Article (R) Number: 580GZ

TI Redox properties of the [2Fe-2S] center in the 24 kDa (NQO2) subunit of
NADH : ubiquinone oxidoreductase (complex I)

AU Zu Y B; Di Bernardo S; Yagi T; Hirst J (Reprint)

CS MRC, Dunn Human Nutr Unit, Wellcome Trust MRC Bldg, Hills Rd, Cambridge
CB2 2XY, England (Reprint); MRC, Dunn Human Nutr Unit, Cambridge CB2 2XY,
England; Scripps Res Inst, Dept Mol & Expt Med, Div Biochem, La Jolla, CA
92037 USA

CYA England; USA

SO BIOCHEMISTRY, (6 AUG 2002) Vol. 41, No. 31, pp. 10056-10069.

ISSN: 0006-2960.

PB AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.

DT Article; Journal

LA English

REC Reference Count: 69

ED Entered STN: 30 Aug 2002

Last Updated on STN: 30 Aug 2002

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The redox proper-ties of the [2Fe-2S] cluster in the 24 kDa subunit of bovine heart mitochondrial NADH:ubiquinone oxidoreductase (complex I) and three of its homologues have been defined using protein-film voltammetry. The clusters in all four examples display characteristic, pH-dependent redox transitions, which, unusually, can be masked by high ionic strength conditions. At low ionic strength (10 mM NaCl) the reduction potential varies by approximately 100 mV between high and low pH limits (pH 5 and 9); thus the redox process is not strongly coupled and is unlikely to form part of the mechanism of energy transduction in complex I. The pH dependence was shown to result from pH-linked changes in protein charge, due to nonspecific protonation events, rather than from the coupling of a specific ionizable residue, and the ionic strength dependence at high and low pH was modeled using extended Debye-Huckel theory. The low potential of the 24 kDa subunit [2Fe-2S] cluster, out of line with the potentials of the other iron-sulfur clusters in complex I, is suggested to play a role in coupling reducing equivalents at the catalytic active site. Finally, the validity of using the [2Fe-2S] cluster in an isolated subunit, as a mechanistic basis for coupled proton-electron transfer in intact complex I, is evaluated.

L7 ANSWER 6 OF 20 SCISEARCH COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 6

AN 2002:770734 SCISEARCH [Full-text](#)

GA The Genuine Article (R) Number: 595BX

TI From NADH to ubiquinone in Neurospora mitochondria

AU Videira A (Reprint); Duarte M

CS Univ Porto, Inst Biol Mol & Celular, Rua Campo Alegre 823, P-4150180

Oporto, Portugal (Reprint); Univ Porto, Inst Biol Mol & Celular, P-4150180

Oporto, Portugal; Univ Porto, Inst Ciencias Biomed Abel Salazar, P-4150180

Oporto, Portugal

CYA Portugal

SO BIOCHIMICA ET BIOPHYSICA ACTA-BIOENERGETICS, (10 SEP 2002) Vol. 1555, No. 1-3, Sp. iss. SI, pp. 187-191. ISSN: 0005-2728.

PB ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.

DT Article; Journal

LA English

REC Reference Count: 64

ED Entered STN: 11 Oct 2002

Last Updated on STN: 11 Oct 2002

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The respiratory chain of the mitochondrial inner membrane includes a proton-pumping enzyme, complex I, which catalyses electron transfer from NADH to ubiquinone. This electron pathway occurs through a series of protein-bound prosthetic groups, FMN and around eight iron-sulfur clusters. The high number of polypeptide subunits of mitochondrial complex I, around 40, have a dual genetic origin. *Neurospora crassa* has been a useful genetic model to characterise complex I. The characterisation of mutants in specific proteins helped to understand the elaborate processes of the biogenesis, structure and function of the oligomeric enzyme. In the fungus, complex I seems to be dispensable for vegetative growth but required for sexual development. *N. crassa* mitochondria also contain three to four nonproton-pumping alternative NAD(P)H dehydrogenases. One of them is located in the outer face of the inner mitochondrial membrane, working as a calcium-dependent oxidase of cytosolic NADPH. (C) 2002 Elsevier Science B.V. All rights reserved.

L7 ANSWER 7 OF 20 SCISEARCH COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 7

AN 2002:826367 SCISEARCH Full-text

GA The Genuine Article (R) Number: 600HM

TI Effect of anoxia/reperfusion on the reversible active/de-active transition of NADH-ubiquinone oxidoreductase (complex I) in rat heart

AU Maklashina E; Sher Y; Zhou H Z; Gray M O; Karlner J S; Cecchini G (Reprint)

CS Vet Adm Med Ctr, Div Mol Biol 151 S, 4150 Clement St, San Francisco, CA 94121 USA (Reprint); Vet Adm Med Ctr, Div Mol Biol 151 S, San Francisco, CA 94121 USA; Univ Calif San Francisco, Dept Biochem & Biophys, San Francisco, CA 94143 USA; Vet Adm Med Ctr, Cardiol Sect, San Francisco, CA 94121 USA

CYA USA

SO BIOCHIMICA ET BIOPHYSICA ACTA-BIOENERGETICS, (3 OCT 2002) Vol. 1556, No. 1, pp. 6-12. ISSN: 0005-2728.

PB ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.

DT Article; Journal

LA English

REC Reference Count: 35

ED Entered STN: 1 Nov 2002

Last Updated on STN: 1 Nov 2002

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The multi-subunit mammalian NADH-ubiquinone oxidoreductase (complex I) is part of the mitochondrial electron transport chain and physiologically serves to reduce ubiquinone with NADH as the electron donor. The three-dimensional structure of this enzyme complex remains to be elucidated and also little is known about the physiological regulation of complex I. The enzyme complex in vitro is known to exist as a mixture of active (A) and de-active (D) forms [Biochim. Biophys.

Acta 1364 (1998) 169]. Studies are reported here examining the effect of anoxia and reperfusion on the A/D-equilibrium of complex I in rat hearts ex vivo. Complex I from the freshly isolated rat heart or after prolonged (1 h) normoxic perfusion exists in almost fully active form (87 +/- 2%). Either 30 min of nitrogen perfusion or global ischemia, decreases the portion of active form of complex I to 40 2%. Upon re-oxygenation of cardiac tissue, complex I is converted back predominantly to the active form (80-85%). Abrupt alternation of anoxic and normoxic perfusion allows cycling between the two states of the enzyme. The possible role in the physiological regulation of complex I activity is discussed. (C) 2002 Elsevier Science B.V. All rights reserved.

L7 ANSWER 8 OF 20 SCISEARCH COPYRIGHT (c) 2008 The Thomson Corporation on STN

AN 2003:229138 SCISEARCH Full-text

GA The Genuine Article (R) Number: 654KJ

TI Quantitative amino acid analysis of bovine NADH: ubiquinone oxidoreductase (Complex I) and related enzymes. Consequences for the number of prosthetic groups

AU Albracht S P J (Reprint); van der Linden E; Faber B W

CS Univ Amsterdam, Swammerdam Inst Life Sci Biochem, Plantage Muidergracht 12, NL-1018 TV Amsterdam, Netherlands (Reprint); Univ Amsterdam, Swammerdam Inst Life Sci Biochem, NL-1018 TV Amsterdam, Netherlands

CYA Netherlands

SO BIOCHIMICA ET BIOPHYSICA ACTA-BIOENERGETICS, (6 MAR 2003) Vol.

1557, No. 1-3, pp. 41-49.

ISSN: 0005-2728.

PB ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.

DT Article; Journal

LA English

REC Reference Count: 67

ED Entered STN: 28 Mar 2003

Last Updated on STN: 28 Mar 2003

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Bovine-heart NADH:ubiquinone oxidoreductase (EC 1.6.5.3; Complex I) is the first and most complicated enzyme in the mitochondrial respiratory chain. Biochemistry textbooks and virtually all literature on this enzyme state that it contains one FMN and at least four iron-sulfur clusters. We show here that this statement is incorrect as it is based on erroneous protein determinations. Quantitative amino acid analysis of the bovine Complex I, to our knowledge the first reported thus far, shows that the routine protein-determination methods used for the bovine Complex I overestimate its protein content by up to twofold. The FMN content of the preparations was determined to be at least 1.3-1.4 mol FMN/mol Complex I. The spin concentration of the electron paramagnetic resonance (EPR) signal ascribed to iron-sulfur cluster N2 was determined and accounted for 1.3-1.6 clusters per molecule of Complex I. These results experimentally confirm the hypothesis [FEBS Lett. 485 (2000) 1] that the bovine Complex I contains two FMN groups and two clusters N2. Also the protein content of preparations of the soluble NAD+-reducing [NiFe]-hydrogenase (EC 1.12.1.2) from *Ralstonia eutropha*, which shows clear evolutionary relationships with Complex I, scores too high by the colorimetric protein-determination methods. Determination of the FMN content and the spin concentration of the EPR signal of the [2Fe-2S] cluster shows that this hydrogenase also contains two FMN groups. A third enzyme (Ech), the membrane-bound [NiFe]-hydrogenase from *Methanosarcina barkeri* which shows an even stronger evolutionary relationship with Complex I, behaves rather normal in protein determinations and contains no detectable acid-extractable FMN in

purified preparations. (C) 2002 Elsevier Science B.V. All rights reserved.

L7 ANSWER 9 OF 20 SCISEARCH COPYRIGHT (c) 2008 The Thomson Corporation on
STN
AN 2002:53937 SCISEARCH [Full-text](#)
GA The Genuine Article (R) Number: 510JE
TI Complex I and Parkinson's disease
AU Greenamyre J T (Reprint); Sherer T B; Betarbet R; Panov A V
CS Emory Univ, Sch Med, Dept Neurol, 1639 Pierce Dr, WMRB 6000, Atlanta, GA
30322 USA (Reprint); Emory Univ, Sch Med, Dept Neurol, Atlanta, GA 30322
USA; Emory Univ, Sch Med, Dept Pharmacol, Atlanta, GA 30322 USA
CYA USA
SO IUBMB LIFE, (SEP-NOV 2001) Vol. 52, No. 3-5, pp. 135-141.
ISSN: 1521-6543.
PB TAYLOR & FRANCIS INC, 325 CHESTNUT ST, SUITE 800, PHILADELPHIA, PA 19106
USA.
DT General Review; Journal
LA English
REC Reference Count: 39
ED Entered STN: 25 Jan 2002
Last Updated on STN: 25 Jan 2002

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Complex I of the mammalian electron transfer chain is composed of at least 43 protein subunits, of which 7 are encoded by mtDNA. It catalyzes the transfer of electrons from NADH to ubiquinone and translocates protons from the mitochondrial matrix to the intermembrane space. It may also play direct roles in the mitochondrial permeability transition and in cell death pathways. Despite the limitations of current complex I assays, biochemical studies have suggested the presence of a mild, systemic defect of complex I in Parkinson's disease (PD). Recent experimental work has modeled this abnormality using rotenone to systemically inhibit complex I. Chronic rotenone exposure accurately recapitulated the pathological, biochemical, and behavioral features of PD. Thus, relatively subtle complex I abnormalities—either genetic or acquired—may be central to the pathogenesis of PD.

L7 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:300133 CAPLUS [Full-text](#)
DN 139:113620
TI The subunit composition of the human NADH dehydrogenase obtained by rapid one-step immunopurification
AU Murray, James; Zhang, Bing; Taylor, Steven W.; Oglesbee, Devin; Fahy, Eoin; Marusich, Michael F.; Ghosh, Soumitra S.; Capaldi, Roderick A.
CS Department of Molecular Biology, University of Oregon, Eugene, OR, 97403, USA
SO Journal of Biological Chemistry (2003), 278(16), 13619-13622
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Defects of the NADH dehydrogenase complex (complex I, NADH-ubiquinone reductase) are predominantly manifested in mitochondrial diseases and are significantly associated with the development of many late onset neuro. disorders such as Parkinson's disease. Here, the authors describe an immunocapture procedure for isolating this multisubunit membrane-bound complex from human tissue. Using small amts. of immunisolated protein, 1-dimensional and 2-dimensional gel electrophoresis, matrix-assisted laser desorption

ionization time-of-flight (MALDI-TOF) peptide mass finger printing (PMF), and nanoflow liquid chromatog. mass spectrometry/mass spectrometry (LC-MS/MS), the authors were able to resolve and identify the human homologs of 42 polypeptides detected so far in the more extensively studied bovine heart complex I. These polypeptides included the GRIM-19 protein, which is claimed to be involved in apoptosis, a polypeptide 1st identified by gene screening as a neuronal protein, as well as a protein thought to be in differentiation-linked processes. The concordance of data from human and bovine complex I isolated by different procedures added to the certainty that these novel proteins of seemingly diverse function are a part of complex I.

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2003:326955 CAPLUS Full-text

DN 139:65304

TI Reversible, electrochemical interconversion of NADH

and NAD⁺ by the catalytic (I_A) subcomplex of
mitochondrial NADH:ubiquinone oxidoreductase (Complex I)

AU Zu, Yanbing; Shannon, Richard J.; Hirst, Judy

CS Dunn Human Nutrition Unit, Medical Research Council, Cambridge, CB2 2XY,
UK

SO Journal of the American Chemical Society (2003), 125(20),
6020-6021

CODEN: JACSAT; ISSN: 0002-7863

PB American Chemical Society

DT Journal

LA English

AB NADH:ubiquinone oxidoreductase (complex I) is the first enzyme of the mitochondrial electron transport chain and catalyzes the oxidation of β -NADH by ubiquinone, coupled to transmembrane proton translocation. It contains a FMN at the active site for NADH oxidation, up to eight iron-sulfur (FeS) clusters, and at least one ubiquinone binding site. Little is known about the mechanism of coupled electron-proton transfer in complex I. This communication demonstrates how the catalytic fragment of complex I, subcomplex I_A, can be adsorbed onto a pyrolytic graphite edge electrode to catalyze the interconversion of NADH and NAD⁺, with the electrode as the electron acceptor or donor. NADH oxidation and NAD⁺ reduction are completely reversible and occur without the application of an overpotential. The potential of zero current denotes the potential of the NAD⁺/NADH redox couple, and the dependence of ENAD⁺ on pH, and on the NADH:NAD⁺ ratio, is in accordance with the Nernst equation. The catalytic potential of the enzyme, E_{cat}, is close to one of the two reduction potentials of the active site FMN and to the potential of a nearby [2Fe-2S] cluster; therefore, either one or both of these redox couples is suggested to be important in controlling NADH oxidation by complex I.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2003:62808 CAPLUS Full-text

DN 138:182889

TI The Proton-Translocating NADH-Quinone Oxidoreductase in the
Respiratory Chain: The Secret Unlocked

AU Yagi, Takao; Matsuno-Yagi, Akemi

CS Department of Molecular and Experimental Medicine MEM-256, Scripps
Research Institute, La Jolla, CA, 92037, USA

SO Biochemistry (2003), 42(8), 2266-2274

CODEN: BICHAJ; ISSN: 0006-2960

PB American Chemical Society
DT Journal; General Review
LA English

AB A review. Topics discussed include structure, substrates and cofactors, inhibitors, accessory subunits and energy coupling of proton-translocating NADH-quinone oxidoreductase.

RE.CNT 92 THERE ARE 92 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:584785 CAPLUS [Full-text](#)
DN 139:212237

TI Profiling genes related to mitochondrial function in mice treated with N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine
AU Gu, Guangyu; Deutch, Ariel Y.; Franklin, Jeff; Levy, Shawn; Wallace, Douglas C.; Zhang, Jing
CS Harborview Medical Center, Department of Pathology, Division of Neuropathology, University of Washington School of Medicine, Seattle, WA, 98104, USA

SO Biochemical and Biophysical Research Communications (2003), 308(1), 197-205
CODEN: BBRC9; ISSN: 0006-291X

PB Elsevier Science
DT Journal
LA English

AB Since mitochondrial dysfunction plays an important role in the pathogenesis of dopaminergic neurodegeneration in Parkinson's disease, we determined the expression of genes related to mitochondrial function in the substantia nigra of mice treated with N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) using a cDNA array. MPTP treatment significantly depleted striatal dopamine, but did not result in apparent neuronal loss in the substantia nigra at 3 and 18 days post-treatment. We also examined changes in genes in the hypothalamus, a region containing dopaminergic neurons that are relatively resistant to MPTP. Finally, we confirmed those genes identified by microarrays as differentially expressed in the substantia nigra but not in the hypothalamus using in situ hybridization. Our results demonstrated that MPTP significantly changed the expressions of six genes in nigral neurons, four of which were related to the mitochondrial electron transport chain: the NADH-ubiquinone oxidoreductase 13 kDa B subunit, the NADH-ubiquinone oxidoreductase MNLL subunit, cytochrome c, and the cytochrome c oxidase Va subunit. Two other differentially expressed genes were the dihydropyridine-sensitive L-type calcium channel α -2 subunit precursor and type III α -1 procollagen. None of these six genes are encoded by mitochondrial DNA. The potential significance of these gene alterations in the context of Parkinson's disease is discussed.

RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:499206 CAPLUS [Full-text](#)
DN 139:242148

TI Mitochondrial complex I from Arabidopsis and rice: orthologs of mammalian and fungal components coupled with plant-specific subunits
AU Heazlewood, Joshua L.; Howell, Katharine A.; Millar, A. Harvey
CS Faculty of Life and Physical Sciences, School of Biomedical and Chemical Sciences, Biochemistry and Molecular Biology, Plant Molecular Biology Group, The University of Western Australia, Western Australia, 6009, Australia

SO Biochimica et Biophysica Acta, Bioenergetics (2003), 1604(3), 159-169

CODEN: BBBEB4; ISSN: 0005-2728

PB Elsevier B.V.

DT Journal

LA English

AB The NADH:ubiquinone oxidoreductase of the mitochondrial respiratory chain is a large multisubunit complex in eukaryotes containing 30-40 different subunits. Anal. of this complex using blue-native gel electrophoresis coupled to tandem mass spectrometry (MS) has identified a series of 30 different proteins from the model dicot plant, Arabidopsis, and 24 different proteins from the model monocot plant, rice. These proteins have been linked back to genes from plant genome sequencing and comparison of this dataset made with predicted orthologs of complex I components in these plants. This anal. reveals that plants contain the series of 14 highly conserved complex I subunits found in other eukaryotic and related prokaryotic enzymes and a small set of 9 proteins widely found in eukaryotic complexes. A significant number of the proteins present in bovine complex I but absent from fungal complex I are also absent from plant complex I and are not encoded in plant genomes. A series of plant-specific nuclear-encoded complex I associated subunits were identified, including a series of ferripyochelin-binding protein-like subunits and a range of small proteins of unknown function. This represents a post-genomic and large-scale anal. of complex I composition in higher plants.

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2002:657834 CAPLUS [Full-text](#)

DN 138:21634

TI Mass spectrometric identification of mitochondrial oxidative phosphorylation subunits separated by two-dimensional blue-native polyacrylamide gel electrophoresis

AU Devreese, Bart; Vanrobaeys, Frank; Smet, Joel; Van Beeumen, Jozef; Van Coster, Rudy

CS Laboratory of Protein Biochemistry and Protein Engineering, Ghent University, Ghent, Belg.

SO Electrophoresis (2002), 23(15), 2525-2533

CODEN: ELCTDN; ISSN: 0173-0835

PB Wiley-VCH Verlag GmbH

DT Journal

LA English

AB Blue-native PAGE is a powerful tool for the separation of intact membrane protein complexes mainly applied to the anal. of the enzymes of the mitochondrial oxidative phosphorylation system (OXPHOS). Combined with SDS-PAGE, it reveals a 2-dimensional pattern showing the individual subunits of the 5 OXPHOS multienzyme complexes. This pattern is useful in the diagnostic anal. of several diseases related to disorders in the oxidative phosphorylation system. However, in order to use this method for systematic diagnostic purposes and to be able to link disease with absence or reduced expression of specific subunits, an unambiguous identification of the individual subunits is necessary. Here, the authors completed this task, implementing peptide mass fingerprinting and mass spectrometric sequence anal. In the course of these analyses, a novel variant of a cytochrome c oxidase subunit VIc was discovered.

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2002:884749 CAPLUS [Full-text](#)

DN 138:268749

TI Cellular distribution of oxygen sensor candidates - oxidases, cytochromes, K⁺-channels- in the carotid body

AU Kummer, Wolfgang; Yamamoto, Yoshio
CS Institute for Anatomy and Cell Biology, Justus-Liebig-University, Giessen,
35385, Germany

SO Microscopy Research and Technique (2002), 59(3), 234-242
CODEN: MRTEEO; ISSN: 1059-910X

PB Wiley-Liss, Inc.

DT Journal; General Review

LA English

AB A review. The specific tissue of the carotid body is built up of groups of glomus cells, enveloped by glial-type sustentacular cells, and innervated by sensory nerve fibers. These units sense arterial pO₂ and respond to hypoxia by a variety of reactions that include initiation of the arterial chemoreflex, i.e., increasing firing activity in the carotid sinus nerve. Until now, neither the cellular localization of the initial events that lead to stimulation of chemoreceptor afferents nor the mol. mechanism of oxygen sensing in the carotid body have been unequivocally identified. Proposed mol. candidates for the mechanism of oxygen sensing include: (1) Components of the mitochondrial respiratory chain, (2) NADPH oxidases generating reactive oxygen species in an oxygen-dependent manner, (3) Oxygen-regulated plasmalemmal K⁺-channels, and (4) Nonoxidase iron-proteins. Our still limited knowledge on their cellular distribution within the carotid body is reviewed here. It is evident that: (1) The distribution of at least some oxygen sensor candidates is not ubiquitous but cell-type-specific, and (2) Each specific parenchymal cell type of the carotid body contains at least one of the proposed oxygen sensor candidates. This applies also for the glial-type sustentacular cells that exhibit immunoreactivity to the two-pore domain K⁺-channel, TASK-1. These observations fit best with the assumption that each cell type within the carotid body is principally responsive to hypoxia. The differential equipping of glomus cells, nerve endings, and sustentacular cells with sensor proteins might serve to determine different thresholds of sensitivity and/or to connect the process of oxygen sensing to different signaling pathways. It also favors the assumption that several mechanisms of oxygen sensing may act simultaneously. The cellular identification of the cell type initiating the chemoreceptor reflex, however, has to await the mol. identification of the particular oxygen sensor mol. that initiates increased carotid sinus nerve activity.

RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2002:821371 CAPLUS [Full-text](#)

DI 138:199252

TI The human complex I NDUFS4 subunit: from gene structure to function and pathology

AU Budde, S. M. S.; van den Heuvel, L. P. W. J.; Smeitink, J. A. M.

CS Nijmegen Centre for Mitochondrial Disorders, Department of Paediatrics,
University Medical Centre Nijmegen, Nijmegen, 6500 HB, Neth.

SO Mitochondrion (2002), 2(1-2), 109-115

CODEN: MITOCN; ISSN: 1567-7249

PB Elsevier Science B.V.

DT Journal; General Review

LA English

AB A review. Complex I is the first and largest enzyme of the oxidative phosphorylation system. It consists of at least 43 subunits. Recent studies have shown that the NDUFS4 subunit of complex I contributes to the activation of the complex through cAMP dependent phosphorylation of a conserved site (RVS) located at the C-terminal region of this protein. This report focuses on the NDUFS4 subunit. Summarized is the current knowledge of this subunit, from gene structure to function and pathol.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2002:668252 CAPLUS Full-text
 DN 138:12511
 TI Yarrowia lipolytica, a yeast genetic system to study mitochondrial complex I
 AU Kersch, Stefan; Drose, Stefan; Zwicker, Klaus; Zickermann, Volker; Brandt, Ulrich
 CS Institut für Biochemie I, Zentrum der Biologischen Chemie, Universitätsklinikum Frankfurt, Frankfurt, D-60590, Germany
 SO Biochimica et Biophysica Acta, Bioenergetics (2002), 1555(1-3), 83-91
 CODEN: BBBEB4; ISSN: 0005-2728
 PB Elsevier B.V.
 DT Journal; General Review
 LA English
 AB A review. The obligate aerobic yeast *Y. lipolytica* is introduced as a powerful new model for the structural and functional anal. of mitochondrial complex I. A brief introduction into the biol. and the genetics of this nonconventional yeast is given and the relevant genetic tools that have been developed in recent years are summarized. The respiratory chain of *Y. lipolytica* contains complexes I-IV, one "alternative" NADH-dehydrogenase (NDH2) and a non-heme alternative oxidase (AOX). Because the NADH binding site of NDH2 faces the mitochondrial intermembrane space rather than the matrix, complex I is an essential enzyme in *Y. lipolytica*. Nevertheless, complex I deletion strains could be generated by attaching the targeting sequence of a matrix protein, thereby redirecting NDH2 to the matrix side. Deletion strains for several complex I subunits have been constructed that can be complemented by shuttle plasmids carrying the deleted gene. Attachment of a hexa-histidine tag to the NUGM (30 kDa) subunit allows fast and efficient purification of complex I from *Y. lipolytica* by affinity-chromatog. The purified complex has lost most of its NADH:ubiquinone oxidoreductase activity, but is almost fully reactivated by adding 400-500 mols. of phosphatidylcholine per complex I. The established set of genetic tools has proven useful for the site-directed mutagenesis of individual subunits of *Y. lipolytica* complex I. Characterization of a number of mutations already allowed for the identification of several functionally important amino acids, demonstrating the usefulness of this approach.

RE.CNT 101 THERE ARE 101 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L7 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2002:726605 CAPLUS Full-text
 DN 138:35870
 TI Characterization of the mitochondrial respiratory pathways in *Candida albicans*
 AU Helmerhorst, Eva J.; Murphy, Michael P.; Troxler, Robert F.; Oppenheim, Frank G.
 CS Goldman School of Dental Medicine, Boston University, Boston, MA, 02118, USA
 SO Biochimica et Biophysica Acta, Bioenergetics (2002), 1556(1), 73-80
 CODEN: BBBEB4; ISSN: 0005-2728
 PB Elsevier B.V.
 DT Journal
 LA English
 AB *C. albicans* is an opportunistic oral pathogen. The flexibility of this microorganism in response to environmental changes includes the expression of a CN--resistant alternative respiratory pathway. In the present study, we

characterized both conventional and alternative respiratory pathways and determined their ADP/O ratios, inhibitor sensitivity profiles, and the impact of the utilization of either pathway on susceptibility to commonly used antimycotics. O₂ consumption by isolated mitochondria using NADH or malate/pyruvate as respiratory substrates indicated that *C. albicans* cells express both cytoplasmic and matrix NADH-ubiquinone oxidoreductase activities. The ADP/O ratio was higher for malate/pyruvate (2.2 ± 0.1), which generate NADH in the matrix, than for externally added NADH (1.4 ± 0.2). In addition, malate/pyruvate respiration was rotenone-sensitive, and an enzyme activity assay further confirmed that *C. albicans* cells express Complex I activity. Cells grown in the presence of antimycin A expressed the CN--insensitive respiratory pathway. Determination of the respiratory control ratio (RCR) and ADP/O ratios of mitochondria from these cells indicated that electron transport from ubiquinone to O₂ via the alternative respiratory pathway was not coupled to ATP production; however, an ADP/O ratio of 0.8 was found for substrates that donate electrons at Complex I. Comparison of antifungal susceptibility of *C. albicans* cells respiring via the conventional or alternative respiratory pathways showed that respiration via the alternative pathway does not reduce the susceptibility of cells to a series of clin. employed antimycotics (using Fungitest), or to the naturally occurring human salivary antifungal peptide, histatin 5.

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:46203 CAPLUS Full-text

DN 142:195161

TI Complex I: structure, function and deficiency

AU Cameron, Jessie M.; Robinson, Brian H.

CS Dept. of Metabolism, Hospital for Sick Children, Toronto, ON, Can.

SO Recent Research Developments in Human Mitochondrial Myopathies (2002), 53-96. Editor(s): Garcia-Trejo, Jose de Jesus. Publisher: Research Signpost, Trivandrum, India.
CODEN: 69GJGW; ISBN: 81-7736-139-2

DT Conference; General Review

LA English

AB A review. NADH:ubiquinone oxidoreductase (complex I) is the first enzyme of the respiratory chain, comprising at least 43 subunits, encoded by both the mitochondrial and nuclear genomes. Despite recent advances in both the elucidation of the enzyme's phys. structure by electron microscopy and the determination of the genetic composition of most of the individual subunits, knowledge of the specific functioning of the enzyme is still largely hypothetical. Complex I deficiency is the greatest cause of neonatal lactic acidosis and Leigh's disease in the general population, and the range of clin. phenotypes produced is unmatched by those from other respiratory chain enzyme defects. While mutations in the mitochondrially encoded subunits were known for some time, the nuclear basis for disease has only recently begun to be delineated. It is now possible to comment on the relationship between mutation and phenotype, and to determine if a clin. consequence can be associated with specific mutations. Eventually this may lead to the possibility of prenatal diagnosis, as well as offering early diagnosis and management therapies for carriers or those with milder phenotypes. Mutations of genes encoding the subunits of complex I appear to account for enzyme defects in only a small proportion of cases, and thus it is this part of the genotypic spectra that is most intriguing. There must be further genes involved that are critical to the correct functioning of the enzyme and it is the identification of these genetic pathways that are the next challenge.

RE.CNT 158 THERE ARE 158 CITED REFERENCES AVAILABLE FOR THIS RECORD
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